

PATENT COOPERATION TREATY

| INTERNATIONAL | APPLICATION | NO. | PCT/GB91 | /00706    |
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| INTERNATIONAL | APPLICATION | NO. | PCT/GB91 | / 00 / 01 |

NOTIFICATION TO THE DESIGNATED TO:

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FILE REFERENCE:

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DATE OF MAILING OF

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NAME(S) OF APPLICANT(S):

COATES, Jonathan, Alan, Victor et al.

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|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|------|------------------------------------------------------------------------------------------------------------------------|
| (21) Int. Application Number                                                                                                                                      | : PCT/GB91/00706                                                                                                                                                                                            | (51) International Patent Classification 5: |      | (11) Int. Publication Number: WO 91/17159                                                                              |
| (22) Int. Filing Date:                                                                                                                                            | 2 May 1991 (02.05.91)                                                                                                                                                                                       | C07D 411/04, A61K 31/505                    | A1   | (43) Int. Publication Date: 14 November 1991 (14.11.91)                                                                |
|                                                                                                                                                                   | 2 May 1990 GB<br>(02.05.90)                                                                                                                                                                                 | (54) Title: 1,3-OXATHIOLANE NUCLEO:         | SIDE | ANALOGUES                                                                                                              |
|                                                                                                                                                                   | TERNATIONAL INC.<br>amon Street, Montreal,                                                                                                                                                                  |                                             |      | iolan-5-yl)-(1H)-pyrimidin-2-one, its pharmaceutically achereof, methods for its preparation and its use as an antivi- |
| Group Research Li<br>Greenford, Middle<br>MUTTON, Ian, M<br>Group Research Li<br>Greenford, Middle<br>PENN, Charles, Rie<br>ER, Richard [GB/<br>Christopher [GB/G | ictor [GB/GB]; Glaxe, mited, Berkley Avenue, sex UB6 0HE (GB). artin [GB/GB]; Glaxo mited, Berkley Avenue, side UB6 0HE (GB). chard [GB/GB]; STOR-GB]; WILLIAMSON, B]; Glaxo Group Redey Avenue, Greenford, |                                             |      |                                                                                                                        |
| (74) Agent: RITTER, Step<br>Squire, 10 Fleet Stro<br>(GB).                                                                                                        | hen, David; Mathys &<br>eet, London EC4Y IAY                                                                                                                                                                |                                             |      | · · · · · · · · · · · · · · · · · · ·                                                                                  |
| BG, BJ (OAPI pate tent), CG (OAPI pate                                                                                                                            | (European patent), AU,<br>nt), BF (OAPI patent),<br>nt), CA, CF (OAPI pa-<br>tent), CH (European pa-<br>ent), CM (OAPI patent),                                                                             | <b>.</b>                                    |      |                                                                                                                        |

DE (European patent), DK (European patent), ES (European patent), FI, FR (European patent), GA (OAPI patent), GB (European patent), GR (European patent), HU, IT (European patent), JP, KR, LK, LU (European patent), ML (OAPI patent), MR (OAPI patent), NL (European patent), NO, PL, RO, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent), US.

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# PATENT COOPERATION TREATY INTERNATIONAL SEARCH REPORT 2 4 SEP 1991

|                                                                                                                                                                                                 | Applicant's or Agent's File Reference                         |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|
| IDENTIFICATION OF THE INTERNATIONAL APPLICATION                                                                                                                                                 | SDR/16160                                                     |
| International Application No.                                                                                                                                                                   | International Filing Date                                     |
| PCT/ GB91/00706                                                                                                                                                                                 | 02/05/91                                                      |
| Receiving Office                                                                                                                                                                                | Priority Date Claimed                                         |
| RO/GB                                                                                                                                                                                           | 02/05/90                                                      |
| Applicant (Name)                                                                                                                                                                                |                                                               |
| IAF BioChem International Inc. et al.                                                                                                                                                           |                                                               |
| I. X CERTAIN CLAIMS WERE FOUND UNSEARCHABLE 1 (Observations on su                                                                                                                               | upplemental sheet (2))                                        |
| II. UNITY OF INVENTION IS LACKING <sup>2</sup> (Observations on supplemental she                                                                                                                | et (2))                                                       |
| III. TITLE, ABSTRACT AND FIGURE OF DRAWING                                                                                                                                                      |                                                               |
| The following indicated items are approved as submitted by the applicant:      X Title.                                                                                                         | g indicated items are set forth below:                        |
| Title. Abstract.                                                                                                                                                                                |                                                               |
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|                                                                                                                                                                                                 | <i>‡</i>                                                      |
| Text of the abstract continued on supplemental sheet (1)  3. a. The definitive contents of the abstract are established by this integration form PCT/ISA/204, previously sent to the applicant. |                                                               |
| b. This report is incomplete as far as the abstract is concerned as the draft prepared by this international Searching Authority has n                                                          | ne time limit for comments by the applicant on oot expired. 4 |
| 4. Figure to be published with the abstract <sup>5</sup>                                                                                                                                        |                                                               |
| Figure No. None of the Figures                                                                                                                                                                  |                                                               |
| as suggested by the applicant because the applicant failed to suggest a figure                                                                                                                  |                                                               |
| because this figure better characterizes the invention                                                                                                                                          |                                                               |

### INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 91/00706

| I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                 |                                       |                          |  |  |
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| According to International Patent Classification (IPC) or to both National Classification and IPC  5 C 07 D 411/04, A 61 K 31/505  IPC:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                 |                                       |                          |  |  |
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| II. FIELD                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Minimum Documen                                                                                                                 | tation Searched 7                     |                          |  |  |
| Classification                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | n System (                                                                                                                      | Classification Symbols                |                          |  |  |
| Classification System   Classification Symbols   C 07 D 411/04, C 07 D 405/04                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                 |                                       |                          |  |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched * |                                       |                          |  |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                 |                                       |                          |  |  |
| III. DOCU                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | MENTS CONSIDERED TO BE RELEVANT                                                                                                 |                                       | D. L A to Claim No. 13   |  |  |
| Category •                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Citation of Document, 11 with Indication, where app                                                                             | ropriate, of the relevant passages 12 | Relevant to Claim No. 13 |  |  |
| A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | EP, A, 0337713 (I.A.F.)<br>18 October 1989<br>see pages 1-5,11; c                                                               | laims                                 | 1,6-9                    |  |  |
| P,X                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | <br>EP, A, 0382526 (I.A.F.)<br>16 August 1990<br>see page 17, exampl<br>claims                                                  | e 7; page 27;                         | 1,6-9                    |  |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                 |                                       |                          |  |  |
| * Special categories of cited documents: 19  *A" document defining the general state of the art which is not considered to be of particular relevance  "E" earlier document but published on or after the international filing date  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or other means  "P" document published prior to the international filing date but later than the priority date claimed  IV. CERTIFICATION  Date of the Actual Completion of the International Search  31st July 1991  International Searching Authority  EUROPEAN PATENT OFFICE  "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention cannot be considered novel or cannot be considered to invention invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents; such combination being obvious to a person skilled in the art.  "&" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such document is combined with one or more other such document is combined with one or more other such document is combined with one or more other such documents is combined with one or more other such documents.  "A" document of particular relevance; the claimed invention cannot be considered to involve an inventive and inventive and invention cannot be considered novel or cannot be considered to involve an inventive and invention cannot be considered novel or cannot be considered |                                                                                                                                 |                                       |                          |  |  |
| 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | EUROPEAN PATENT OFFICE                                                                                                          | [//                                   | . 765                    |  |  |

| i                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1                                                                                                                                                        | -                                          |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | PE FOUND UNSEARCHABLE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                          |                                            |
| OBSERVATIONS WHERE CERTAIN CLAIMS WE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | RE FOURD CITED TO THE PROPERTY OF THE PROPERTY | and the transfer following const                                                                                                                         | 008:                                       |
| s international search report has not been established in re                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | spect of certain claims under Article                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 17(2) (a) for the following reco-                                                                                                                        | )                                          |
| * Claim numbers 10 because they relate to subject n                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | natter not required to be searched b                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | y this Authority, namely:                                                                                                                                | 1                                          |
| _                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                          |                                            |
| Pls. see Rule 39.1(iv) - PCT:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                          | -                                          |
| Methods for treatment of the huma                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | an or animal body by                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | therapy or surge                                                                                                                                         | ry                                         |
| as well as diagnostic methods.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ·                                                                                                                                                        |                                            |
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| Claim numbers, because they relate to parts of                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                          |                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | al search can be carried out, specific                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                          |                                            |
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| Claim numbers, because they are dependent cla<br>PCT Rule 6.4(a).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | ims and are not drafted in accordanc                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                          | tences of                                  |
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#### ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO.

GB 9100706 SA 47177

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 27/08/91

The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

| Patent document cited in search report | Publication<br>date |                         | t family<br>iber(s)           | Publication<br>date              |
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| EP-A- 0337713                          | 18-10-89            | AU-A-<br>JP-A-          | 3264489<br>1316375            | 12-10-89<br>21-12-89             |
| EP-A- 0382526                          | 16-08-90            | AU-A-<br>CA-A-<br>JP-A- | 4920190<br>2009637<br>3007282 | 16-08-90<br>08-08-90<br>14-01-91 |

## INTERNATIONAL APPLICATION UNDER THE PATENT COOPERATION TREATY

REQUEST ,

THE UNDERSIGNED REQUESTS THAT THE PRESENT INTERNATIONAL APPLICATION BE PROCESSED ACCORDING TO THE PATENT COOPERATION TREATY

| 1  |                                           |                                                                      |
|----|-------------------------------------------|----------------------------------------------------------------------|
|    | (The following in INTERNATION APPLICATION | s to be filled , the receiving Office;  NAL N No: 957/25 9 1 2 5 7 3 |
|    | INTERNATIO<br>FILING DATE                 | NAL                                                                  |
|    | (Siamp)                                   | United Kingdom Patent Office<br>PCT International Application        |
|    | Name of receivi                           | ng Office and "PCT International Application"                        |
|    | Applicant's or A<br>(indicated by ap      | Agent's File Reference SDR/16160 pitcant if desired)                 |
| т, | OT AND MITCED                             | OCTRE ANALOGUES                                                      |

|                                                                                                                                    | (i                                                | ndicated by applicant if desire                       | ed) 2DK/10100                                  |
|------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|-------------------------------------------------------|------------------------------------------------|
| Box No. 1 TITLE OF INVENTION                                                                                                       | 1,3-OXATHIOLA                                     | ANE NUCLEOSIDE AN                                     | ALOGUES                                        |
|                                                                                                                                    |                                                   |                                                       | <del></del>                                    |
|                                                                                                                                    |                                                   |                                                       |                                                |
| Box No. II APPLICANT (WHETHER (APPLICANT. Use this box for indicating thapplicable, a legal entity) is involved, contin            |                                                   | TOR); DESIGNATED ST<br>everal applicants, one of them | ATES FOR WHICH HE/SHE/IT IS                    |
| The person identified in this box is (check o                                                                                      |                                                   | nt and inventor*                                      | X applicant only                               |
| Name and address:**                                                                                                                |                                                   |                                                       | applicant only                                 |
|                                                                                                                                    |                                                   | International Inc                                     |                                                |
|                                                                                                                                    | 10900 Hamon S<br>Montreal, Que                    |                                                       |                                                |
|                                                                                                                                    | H3M 3A1                                           | .500                                                  |                                                |
|                                                                                                                                    | CANADA                                            |                                                       |                                                |
|                                                                                                                                    |                                                   |                                                       |                                                |
| Telephone number:<br>(including area code)                                                                                         | Telegraphic address:                              | Teleprin                                              | nter address:                                  |
| Country of nationality: CA                                                                                                         |                                                   | Country of residence:***                              | CA                                             |
| The person identified in this box is applican                                                                                      |                                                   | k one only):                                          |                                                |
| all designated States X all designated University                                                                                  | gnated States except<br>ited States of America    | the United States of America only                     | the States indicated in the "Supplemental Box" |
|                                                                                                                                    |                                                   |                                                       |                                                |
| Box No. III FURTHER APPLICANTS (IF applicable, a legal entity). If the following two tional person the same indications as those r | o sub-boxes are recommendation                    | rate sub-box has to be tilled in i                    | in respect of each person ( includes, where    |
| The person identified in this sub-box is (chec                                                                                     |                                                   | icant and inventor                                    | applicant only inventor only                   |
| Name and address:**                                                                                                                |                                                   |                                                       | ·                                              |
|                                                                                                                                    |                                                   | han Alan Victor<br>esearch Limited                    |                                                |
|                                                                                                                                    | Berkley Avenu                                     |                                                       |                                                |
|                                                                                                                                    | Middlesex UB6                                     |                                                       | •                                              |
|                                                                                                                                    | ENGLAND                                           |                                                       |                                                |
| Make a super day of the state of the                                                                                               | 4.3.                                              |                                                       |                                                |
| If the person identified in this sub-box is app                                                                                    | plicant (or applicant and in                      |                                                       |                                                |
| Country of nationality: GB                                                                                                         | •                                                 | Country of residence:***                              | GB                                             |
| and whether that person is applicant for the                                                                                       | ourposes of (check one on<br>gnated States except |                                                       | ,                                              |
| the Uni                                                                                                                            | ited States of America                            | x the United States of America only                   | the States indicated in the "Supplemental Box" |
| The person identified in this sub-box is (chec                                                                                     | k one only): X appl                               | licant and inventor                                   | applicant only inventor only                   |
| Name and address: **                                                                                                               |                                                   | <del></del>                                           | <del></del>                                    |
|                                                                                                                                    | MUTTON; Ian M                                     |                                                       |                                                |
|                                                                                                                                    | Berkley Avenu                                     | esearch Limited                                       |                                                |
|                                                                                                                                    | Middleside UB6                                    |                                                       |                                                |
|                                                                                                                                    | ENGLAND                                           |                                                       |                                                |
| If the annual administration is the second                                                                                         | a.B.                                              |                                                       |                                                |
| If the person identified in this sub-box is app  Country of nationality:  GB                                                       | olicant (or applicant and in                      |                                                       |                                                |
|                                                                                                                                    |                                                   | Country of residence:                                 | GB                                             |
| and whether that person is applicant for the s                                                                                     | Rnated States except                              |                                                       | The States in discord                          |
| all designated States all designated States the Uni                                                                                | ted States of America                             | the United States of America only                     | the States indicated in the "Supplemental Box" |
| If the person indicated as "applicant angive the necessary indications in the "S                                                   | d inventor" or as "invento<br>upplemental box."   | r only" is not an inventor for t                      | he purposes of all the designated States.      |

Indicate the name of a natural person by giving his/her family name first followed by the given name(s). Indicate the name of a legal entity by its full official designation. In the address, include both the postal code (if any) and the country (name).

| The person identified in this sub-box is (check one only):     X   applicant and inventor*   applicant only   inventor only*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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| PENN; Charles Richard Glaxo Group Research Limited Berkley Avenue, Greenford Middlesex UB6 OHE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Glaxo Group Research Limited Berkley Avenue, Greenford Middlesex UB6 OHE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
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| G.B.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| If the person identified in this sub-box is applicant (or applicant and inventor), indicate also:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Country of residence:***                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| and whether that person is applicant for the purposes of (check one only):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| in the Supplemental Box                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| The person identified in this sub-box is (check one only): X applicant and inventor applicant only inventor only                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
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| STORER; Richard                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Glaxo Group Research Limited                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Berkley Avenue, Greenford                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
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| If the person identified in this sub-box is applicant (or applicant and inventor), indicate also:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
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| and whether that person is applicant for the purposes of (check one only):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| all designated States all designated States except the United States of America the United States of America the "Supplemental Box"                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| WILLIAMSON; Christopher                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Glaxo Group Research Limited                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
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| If the person identified in this sub-box is applicant (or applicant and inventor), indicate also:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
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| If the person identified in this sub-box is applicant (or applicant and inventor), indicate also:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
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| all designated States   all designated States except   the United States   the United |
| If the person indicated as "applicant and inventor" or as "inventor only" is not an inventor for the purposes of all the designated States.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| ** Indicate the name of a natural person by giving his/her family name first followed by the given name(s). Indicate the name of a legal entity by its full official designation. In the address, include both the postal code (if any) and the country (name).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| *** If residence is not indicated, it will be assumed that the country of residence is the same as the country indicated in the address.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| If this continuation sheet is not used, it need not be included in the Request.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

| BOY NO IV ACENT (IF ANY) OR COMMON REPRESENTA                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Day No. IV. ACENT (IF ANN) OF COMMON PERPECCIONAL                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |  |  |  |  |
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| Box No. IV AGENT (IF ANY) OR COMMON REPRESENTATIVE (IF ANY); ADDRESS FOR NOTIFICATIONS (IN CERTAIN CASES). A common representative may be appointed only if there are several applicants and if no agent is or has been appointed; the common representative must be one of the applicants.  The following person (includes, where applicable, a legal entity) is hereby/has been appointed as agent or common representative to act on behalf of the applicant(s) before the competent international Authorities: |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |  |  |  |
| Name and address, including postal code and country:  If the space below is used instead for an address for notifications, mark here                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |  |  |  |
| RITTER; Stephen David  MATHYS & SQUIRE  10 FLEET STREET  LONDON, EC4Y 1AY C.B.                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |  |  |  |
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| Telephone number: 071-353-2491 Telegraphic 24827 (including area code) address:                                                                                                                                                                                                                                                                                                                                                                                                                                    | Teleprinter 071-583-0528                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |  |  |  |
| Box No. V DESIGNATION OF GROUPS OF STATES OR SOR TREATMENT. The following designations are hereby made (p                                                                                                                                                                                                                                                                                                                                                                                                          | TATES (1): CHOICE OF CERTAIN VINDS OF PROTECTION                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  |  |  |  |
| Regional Patent                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | The second contract of |  |  |  |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | CH and LI Switzerland and Liechtenstein. DE Germany FR France, GB United Kingdom, IT Italy, LU Luxembourg, uropean Patent Convention and of the PCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |  |  |  |  |
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| 1 0 4 4 4                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | and of the PCT; if other OAPI title desired, specify on dotted line(3):                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |  |  |  |  |
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| DE Germany (Federal Republic of)(3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | X NO Norway                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |  |  |  |  |
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| ES Spain <sup>(3)</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | SE Sweden                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |  |  |  |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ent) which have become party to the PCT after the issuance of this sheet:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  |  |  |  |
| PL PO (Poland) EP (European Patent): GR Greece                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |  |  |  |  |
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|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | cated by marking the check-boxes with sequential arabic numerals (see                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |  |  |  |  |
| (2) The selection of particular States for a European patent can be n Patent Office (see also the "Notes to Box No. V")                                                                                                                                                                                                                                                                                                                                                                                            | made upon entering the national (regional) phase before the European                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |  |  |  |  |
| (3) If another kind of protection or a title of addition or, in the United<br>is desired, specify according to the instructions given in the "No                                                                                                                                                                                                                                                                                                                                                                   | States of America, treatment as a continuation or a continuation-in-part                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |  |  |  |  |
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| Box No. VI PRIORITY CLAI                                                                                                                              | IM (IF ANY). The priorit                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | ty of the following e                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | arlier application(s) is                                                                                                                                               | hereby claimed:                                                                                                               |
| Country (country in which it was filed if national application: one of the countries for which it was filed if regional or international application) | Filing Date (day, month, yea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Application No.                                                                                                                                                        | Office of Filing (fill in only if<br>the earlier application is an<br>international application<br>or a regional application) |
| (1) GB                                                                                                                                                | 2nd MAY 19                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 990                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 9009861.7                                                                                                                                                              |                                                                                                                               |
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| (3)                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                        |                                                                                                                               |
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| the receiving Office is herebearlier application/of the ear                                                                                           | by requested to prepare an irlier applications identified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | nd transmit to the Ind<br>d above by the numb                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | nternational Bureau a c<br>bers (insert the applica                                                                                                                    |                                                                                                                               |
| Box No. VII EARLIER SEAR<br>Searching Authority has already to<br>to the extent possible, on the res-<br>tion (or the translation thereof) or         | sults of the said earlier sea                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | ech Identify such a                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | rnational, international<br>Authority is now reque<br>earch or request either                                                                                          | al-type or other) by the international<br>ested to base the international search,<br>ir by reference to the relevant applica- |
| International application number number and country (or regional Office) of other application:                                                        | or                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Intern<br>filing                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | national/regional/natio<br>date                                                                                                                                        | onal                                                                                                                          |
| Date of request for search:                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | ber (if available)<br>to search request:                                                                                                                               |                                                                                                                               |
| If the present Request form is sign<br>the applicant is required. If in such<br>thereof must be attached to this fo                                   | R; Stephen David and applicate the case it is desired to make form.  To be filled in by the Application of the contains the following number of the contains the contain | rant by an agent, a see e use of a general portant)  This check in the | sinternational application international application is separate signed power copy of general power priority document(s) receipt of the fees paid cheque for the payme | r of attorney  (see Box No. VI)  id or revenue stamps  ent of fees                                                            |
| Figure number o to accompany the abstract for p                                                                                                       | Total 36  of the drawings (if any) is suppublication.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | sheets 6                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | other document (spec<br>FORM 51/77;                                                                                                                                    | cify)                                                                                                                         |
|                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | to be filled in by the s                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | receiving Office)                                                                                                                                                      |                                                                                                                               |
| Date of actual receipt of the pure.     Corrected date of actual receipt.                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | <u> </u>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | May 19                                                                                                                                                                 | 191 02-05-91                                                                                                                  |
| or drawings completing the pur                                                                                                                        | rported international applic                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | cation:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                                                                                                                        |                                                                                                                               |
| Date of timely receipt of the rec     Drawings Received                                                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | article 11 of the PCT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Γ:                                                                                                                                                                     |                                                                                                                               |
| 4. Diawings                                                                                                                                           | No Drawings                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                                                                                        |                                                                                                                               |
| Date of receipt of the record copy:                                                                                                                   | (The following is to b                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | / _                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 1. 05. 91                                                                                                                                                              |                                                                                                                               |

### INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 91/00706 1. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) According to International Patent Classification (IPC) or to both National Classification and IPC C 07 D 411/04, A 61 K 31/505 5 II. FIELDS SEARCHED Minimum Documentation Searched 7 Classification System Classification Symbols 10 IPC<sup>5</sup> C 07 D 411/04, C 07 D 405/04 Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched 15 III. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of Document, 11 with Indication, where appropriate, of the relevant passages 12 Relevant to Claim No. 13 Category . 20 EP, A, 0337713 (I.A.F.) А 1,6-9 18 October 1989 see pages 1-5,11; claims 25 P,X . EP, A, 0382526 (I.A.F.) 1,6-9 16 August 1990 see page 17, example 7; page 27; claims "T" later document published after the international filing date or priority date and not in conflict with the explication but cited to understand the principle or theory underlying the Special categories of cited documents: 19 document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international filing date document of particular relevance: the claimed invention cannot be considered novel of cannot be considered to involve an inventive step document which may throw goubts on pnormy claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person sailled in the art. 50 "O" document referring to an oral disclosure, use, exhibition or document sublished snor to the international filling date but later than the priority date claimed "4" document member of the same patent family IV. CERTIFICATION Date of Mailing of this International Search Report Date of the Actual Completion of the International Search 55 - 2. 09. 91 31st July 1991 resulte between Authorized Officer International Searching Authority M. PEIS EUROPEAN PATENT OFFICE

International Application No. PCT/GB 91/00706

| <b>.</b>     | FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET                                                                                                                                                                             |  |  |  |  |  |
|--------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--|--|--|--|
| <b>8</b> ··• |                                                                                                                                                                                                                                 |  |  |  |  |  |
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| 5            |                                                                                                                                                                                                                                 |  |  |  |  |  |
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| 10           |                                                                                                                                                                                                                                 |  |  |  |  |  |
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| 15           |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              | VIX OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE                                                                                                                                                                   |  |  |  |  |  |
| 2.0          | This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:  1. Claim numbers                                                                     |  |  |  |  |  |
| 20           | Pls. see Rule 39.1(iv) - PCT:                                                                                                                                                                                                   |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              | Methods for treatment of the human or animal body by therapy or surgery as well as diagnostic methods.                                                                                                                          |  |  |  |  |  |
| 25           |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              | 2. Claim numbers, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: |  |  |  |  |  |
| 2.0          |                                                                                                                                                                                                                                 |  |  |  |  |  |
| 30           |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
| 35           | 3. Claim numbers because they are dependent claims and are not drafted in accordance with the second and third sentences                                                                                                        |  |  |  |  |  |
|              | PCT Ruse 6.4(a),                                                                                                                                                                                                                |  |  |  |  |  |
|              | VI OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING :                                                                                                                                                                           |  |  |  |  |  |
| 40           | This international Searching Authority found multiple inventions in this international application as follows:                                                                                                                  |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
| 45           | 1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.                                                    |  |  |  |  |  |
| ٠.           | 2. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only                                                                                          |  |  |  |  |  |
|              | these claims of the international application for which loss were said, specifically claims:                                                                                                                                    |  |  |  |  |  |
| 50           |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              | 2. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims: it is covered by claim numbers:           |  |  |  |  |  |
|              |                                                                                                                                                                                                                                 |  |  |  |  |  |
|              | 4. As all searchable claims could be searched without effort justifying an additional les, the international Searching Authority did not                                                                                        |  |  |  |  |  |
| 55           | Remark on Protect                                                                                                                                                                                                               |  |  |  |  |  |
|              | The additional search less were accompanied by applicant's protect.                                                                                                                                                             |  |  |  |  |  |
|              | No present accompanied the payment of additional search local                                                                                                                                                                   |  |  |  |  |  |
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This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 27/08/91. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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